

Application No. 09/938,763

RD-28250

**REMARKS**

Claims 1 to 7, 9 to 10, 13 to 15, 17 to 36 and 39 to 42 are pending.

**I. REJECTION OF CLAIMS 1 TO 7, 9 TO 10, 13 TO 36 AND 39 TO 42 UNDER 35 U.S.C. 112, SECOND PARAGRAPH**

Claims 1 to 7, 9 to 10, 13 to 36 and 39 to 42 were rejected under 35 U.S.C. §112, second paragraph.

The claims have been amended to substitute "greater or less than the standard deviation" for outside the standard deviation. It is believed that the PTO is proposing this change by including the parenthetical "greater or less than" in the body of the rejection. Hence, the amendment should overcome the rejection.

Claim 10 has been amended to correct the variable at the end of (iii).

The rejection of claims 1 to 7, 9 to 10, 13 to 36 and 39 to 42 under 35 U.S.C. §112, second paragraph should be withdrawn.

**II. REJECTION OF CLAIM 16 UNDER 35 U.S.C. 112, FIRST PARAGRAPH**

Claim 16 was rejected under 35 U.S.C. 112, first paragraph. Claim 16 has been canceled to overcome the rejection.

**III. 35 U.S.C. 103(a) REJECTIONS**

Claims 1 to 7, 9, 10, 13 to 28, 34 to 36 and 39 to 42 were rejected under 35 U.S.C. 103(a) over Agrafiotis et al. and Grate et al. and claims 1 to 7, 9, 10, 13 to 36 and 39 to 42 were rejected under 35 U.S.C. 103(a) over Agrafiotis et al., Grate et al. and Chaudhari et al.

**A. REJECTION BURDEN OF PROOF**

First, the Office Action states that "Applicant's argument has been fully considered and found to be unpersuasive." Office Action page 6. However, this is not the issue. The 35 U.S.C. 103(a) rejections are based on 35 U.S.C. 102(a) stating "A

Application No. 09/938,763

RD-28250

person shall be entitled to a patent *unless* (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent..." (emphasis added). A patent must be issued *unless* the PTO establishes a reason not to issue the patent; for example, by establishing a *prima facie* case of obviousness. With respect to a *prima facie* case, MPEP 2142 points out that:

.... The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness.

MPEP 2142.

Hence, the issue is not whether "Applicant's argument has been .... found to be unpersuasive." The issue is whether the PTO has met its burden of establishing a *prima facie* case of obviousness. In this case, the PTO has not met this burden. (1) The rejections are based on "non-analogous" art. (2) The rejections are based on improper combinations of references without the motivation to combine required by *In re Lee*, 277 F.3d 1338, 61 USPQ 2d 1430 (Fed. Cir. 2002). (3) Even improperly combined, the references do not make out a *prima facie* case of obviousness. See *In re Deuel*, 34 USPQ2d 1210 (Fed. Cir. 1995). The rejections should be withdrawn.

#### **B. IMPROPER COMBINATION OF REFERENCES-NON ANALOGOUS ART**

Applicant's October 22, 2003 Request for Reconsideration pointed out:

The Agrafiotis et al reference relates to a synthesis protocol with reiterated synthesis steps based on "structure-activity models" (Abstract). Grate et al. discloses "analyzing [a] sample with a multivariate instrument," for example, acoustic wave sensors (col. 9, lines 56 to 65). Chaudhari et al. is a commonly assigned patent that teaches reacting a hydroxyaromatic compound with oxygen and carbon monoxide in the presence of a VIIIIB catalyst to synthesize a diaryl carbonate (Abstract). The invention is a method of defining an experimental space for a CHTS method (claim 1).

The PTO has not provided the "reason to combine" showing required by *In re Lee*, 277 F.3d 1338, 1343, 61 USPQ 2d 1430, 1433-1434 (Fed. Cir.

Application No. 09/938,763

RD-28250

2002) to support a combination of references rejection. A reference that teaches only "analyzing [a] sample with a multivariate instrument" (Grate et al.) and a diaryl carbonate synthesis method are not "reasonably pertinent" to a method of defining an experimental space for a CHTS method. The references are not properly combinable with the Agrafiotis et al reference as analogous art. See *In re Clay*, 23 USPQ2d 1058, 1060 (Fed. Cir. 1992).

October 22, 2003 Request for Reconsideration page 9.

The Applicant has examined the present Office Action but has been unable to identify any response to the "non-analogous" *In re Clay* requirement requisite to combining references to support a rejection. The PTO's attention is respectfully directed to 37 CFR 1.104 entitled "Nature of examination," which states "(b) *Completeness of examiner's action*. The examiner's action will be complete as to all matters...." Further, MPEP 707.07, entitled "Completeness and Clarity of Examiner's Action," provides that "[t]he examiner must address all arguments which have not already been responded to in the statement of the rejection." Further MPEP 707.07(f) entitled "Answer All Material Traversed" states "Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicant's argument and answer the substance of it."

The PTO has failed to point out how "analyzing [a] sample with a multivariate instrument," for example, acoustic wave sensors art (Grate et al.) is analogous to CHTS. The PTO has failed to point out how the "diaryl carbonate" synthesis art (Chaudhari et al.) is analogous to CHTS. The PTO is requested to withdraw the rejections and allow the claims or to reissue another Office Action that responds to Applicant's "non-analogous" *In re Clay* argument.

### **C. IMPROPER COMBINATION OF REFERENCES-NO REASON TO COMBINE**

To support a rejection based on a combination of references, "[t]he PTO "must not only assure that... requisite findings are made, based on evidence of record, but must also *explain the reasoning by which the findings are deemed to support the agency's conclusion*" (emphasis added). *In re Lee*, *supra* 61 USPQ 2d at 1434, 277 F.3d at 1343

Application No. 09/938,763

RD-28250

(Fed. Cir. 2002).

In response to this important requirement, the October 29 Office Action states:

Agrafiotis et al. discloses a system and method for efficiently and effectively generating new leads (identifying) (column 3, lines 27-29) with improved activity and properties (column 4, lines 7-12) by analyzing the leads compounds to identify which of said compounds were adequately synthesized, and which of the compounds were not adequately synthesized based on chemical data (classification) (column 6, lines 2-20).

and then argues:

The improvement disclosed by Agrafiotis et al, as cited above provides sufficient motivation to one of ordinary skill to improve on said method by using a matrix algebra for characterizing, classifying, and identifying chemicals in a sample as taught by Grate et al. (Column 14, equation 10).

and:

Further, the said disclosure of Agrafiotis et al. sufficiently motivates of one of ordinary skill to improve on the said method of Agrafiotis et al. and Grate et al. for using a matrix algebra to characterize, classify, and identify chemicals in a sample using a palladium, halide or co-catalysts as taught by Chaudhari et al.

Office Action page 7.

But these arguments are only conclusions without logic. Merely stating that the Agrafiotis et al. teaching provides motivation is not the *In re Lee* reasoning required to support a combination rejection. Why does "[t]he improvement disclosed by Agrafiotis et al. (generating new leads) provide motivation to use matrix algebra? Why does "[t]he improvement disclosed by Agrafiotis et al. (generating new leads) provide motivation for application to a carbonylation synthesis? There is no teaching whatsoever in the references of a need to improve on a CHTS method by "using a matrix algebra for characterizing, classifying, and identifying chemicals in a sample."

There is no teaching whatsoever in the references of a need to improve on a carbonylation method by "using a matrix algebra analyzed CHTS experiment. To the contrary, the teachings to apply matrix algebra "for characterizing, classifying..." appear

Application No. 09/938,763

RD-28250

solely in Applicant's specification-not in the prior art. And the teachings to apply matrix algebra to a carbonylation CHTS method appear solely in Applicant's specification-not in the prior art. The rejections are based on a selective picking and choosing of features in secondary references, without any basis in the references for doing so. The rejections are supportable only through hindsight. See *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

The PTO has not establish that the references are analogous art and has failed to provide the required *In re Lee* reasoning to combine. The combination rejections of claims 1 to 7, 9, 10, 13 to 28, 34 to 36 and 39 to 42 under 35 U.S.C. 103(a) over Agrafiotis et al. and Grate et al. and claims 1 to 7, 9, 10, 13 to 36 and 39 to under 35 U.S.C. 103(a) over Agrafiotis et al., Grate et al. and Chaudhari et al. should be withdrawn.

#### D. NO PRIMA FACIE CASE

The claims have been amended to further define factors as comprising "a catalyst system and conditions." Support for these amendments is found in the EXAMPLES and in the specification generally. Even improperly combined, the references do not establish a prima facie case of obviousness of (1) defining an experimental space of a catalyzed chemical reaction to represent at least three factor interactions, "wherein the factors comprise a catalyst system and conditions" (all claims).

Additionally as previously argued, the references do not establish a prima facie case of (2) analyzing combinatorial results according to matrix algebra to select a best case set of factor levels from a *catalyzed experimental space* (claims 1 to 7 and 18 to 33); (3) conducting a CHTS on qualitative and quantitative factors (claim 35); (4) a programmed controller that analyzes CHTS results *according to matrix algebra* (claims 36, 39 and 41); (5) defining a space to represent "at least 6 orders of interaction of factors" of a *catalyzed chemical reaction* (claim 5); (5) defining a space to represent "at least 6 orders of interaction of factors" of a *catalyzed chemical reaction* (claim 6); (6) analyzing *combinatorial results* according a relationship  $y = X\beta + e$  where X is a matrix of experiment factor and interaction levels, y is a matrix of experimental results,  $\beta$

Application No. 09/938,763

RD-28250

is effects and  $e$  is an error term of variance  $\sigma^2$  from a normal distribution (claim 18); (7) assembling results as an  $n \times 1$  vector  $y$ , assembling factor level values into an  $n \times k+1$  matrix  $X$ , representing extents of the results and factor level values as +1's and -1's accordingly and solving for *effects parameters*  $\beta$  according to the relationship  $\beta = (X'X)^{-1}X'y$  where superscript  $'$  is a transpose of a matrix and superscript  $-1$  identifies an inverse function of a matrix (claims 19 to 21); (8) reacting and identifying tagged reactants and products (claim 25); (9) reiterating a CHTS on an experimental space selected by matrix algebra analysis of first iteration results (claims 26 to 28); and (10) defining an experimental space to "comprise a reactant or catalyst at least partially embodied in a liquid and... contacting the reactant or catalyst with an additional reactant at least partially embodied in a gas, wherein the liquid forms a film having a thickness sufficient to allow a reaction rate that is essentially independent of a mass transfer rate of additional reactant into the liquid to synthesize products that comprise the results" (claim 34).

Applicant has presented arguments (2) through (10) in his October 22, 2003 Request for Reconsideration. The PTO has not responded.

While the Office Action does mentions some of the key words in Applicant's argument, the October 29 Office Action fails to properly address the invention as defined by the claims. For example, the Office Action states:

The system of Agrafiotis et al. comprises a processor and controller (Figure 1) wherein the reactions occur defined space of 96 well plates (column 20, lines 51-67), and a detection device (column 10, lines 5-14), as in instant claims 39-42.

Office Action page 8.

However, claim 39 does not just claim a "controller." Claim 39 claims a "programmed controller that (A) represents the results as an  $n \times 1$  matrix  $y$  where  $n$  = a number of factor level combinations in the experiment; (B) represents extents of the factor level combinations in an  $n \times n$  matrix  $X$ ; (C) solves  $n$  simultaneous equations represented by the matrices according to matrix algebra to form a results matrix  $\beta$ ; (D) represents the results matrix  $\beta$  as a normal probability plot; (E) defines a standard deviation for a result of the plot wherein the standard deviation represents a probability

Application No. 09/938,763

RD-28250

that a result deviation from the standard is random and that a positive interaction can be identified greater or less than the deviation; and (F) identifies the positive interaction greater or less than the standard deviation to identify an effect greater or less than the standard deviation that represents a best case set of factor levels from the catalyzed experimental space." This is not the Agraftotis et al. processor or controller.

Further, the PTO argues:

It is re-iterated that Agraftotis et al. discloses a method of defining an experimental space such as a combinatorial chemical library where a combinatorial chemical library could be constructed from chemical building blocks designated as A, B, and C. Further, the compounds in the combinatorial chemical library are equal to two in length, then, the compounds would be generated are: AA, AB,...and CC (total of nine) (column 5, lines 5-18), as in instant claims 2, 3, and 5-7.

Office Action page 7 to 8.

But A, B, C.... building blocks are not factors of a "catalyst system."

"A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art...." *In re Rijckaert*, 28 USPQ2d 1955, 1956 (Fed. Cir. 1992). Agraftotis et al., Grate et al. and Chaudhari et al. fail to teach or suggest any of (1) through (11) above. "If examination... does not produce a prima facie case of unpatentability, then without more the applicant is entitled to grant of the patent." *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).

Again, with respect to all of (1) through (10), the Office Action fails to point out where teachings of these limitations appear in the prior art references. Indeed, (1) through (10) do not appear in the references. The PTO has not established a prima facie case of obviousness of (1) through (10).

The PTO is respectfully requested to allow the claims or withdraw the present office action and to issue a new non-final office action that responds to all Applicant's arguments, restarting the period for response.

Application No. 09/938,763

RD-28250

#### IV. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that claims 1 to 7, 9 to 10, 13 to 15, 17 to 36 and 39 to 42 are allowable. Reconsideration and allowance are requested.

Should the Examiner believe that any further action is necessary in order to place this application in condition for allowance, he is requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,



Philip D. Freedman

Reg. No. 24,163

Philip D. Freedman PC

Customer Number 25101

6000 Wescott Hills Way

Alexandria, Virginia 22315-4747

(703) 313-0171

Fax: (703) 313-9322

Email: tekesq@tekesq.com

Alexandria, Virginia  
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